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SENSITIVITY TO HYDROCORTISONE ACETATE OINTMENT

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"*But ne'er the rose without the thorn.*" (Herrick.)

With the introduction of hydrocortisone as an application for eczematous conditions of the skin, it seemed that we had at last achieved a rational form of dermatological therapy, free from any danger of sensitizing the skin. However, reports of sensitivity to hydrocortisone ointments have already been published (Burckhardt, 1959 ; Kooij, 1959). The following is an account of five patients encountered in the space of ten months, who developed a sensitization reaction to a form of hydrocortisone acetate ointment.

Case Records.

Case 1.—A man aged 47 had suffered from otitis externa for four years when he was first treated with hydrocortisone acetate ointment *Z*. He responded rapidly to treatment and after three months was returned to the care of his own doctor to continue the same treatment. Six weeks later he was again seen, the eruption on the ears having flared up severely. He also had a square patch of dermatitis on the left eyelids where he had applied the same ointment to allay irritation. Patch tests to hydrocortisone acetate ointment *Z* produced a weeping erythema ; the base produced no reaction. Treatment with hydrocortisone acetate lotion prepared by a different process healed the eruption in six weeks and he has remained well since.

Case 2.—A woman aged 53 had suffered from eczema of the hands, arms and face for many years and had attended this department since 1947. In August 1955 she first used hydrocortisone acetate ointment *Z* and during 1956 and 1957 the same ointment with the addition of neomycin. In February 1958 she had a severe relapse and had to be admitted to hospital. The same hydrocortisone-neomycin application was continued and the eruption steadily worsened. With the reaction of Case 1 in mind, the local application was changed to hydrocortisone acetate lotion *X*. With this change she steadily improved and was discharged from hospital four weeks later. She has continued using this lotion and her skin eruption has been satisfactorily controlled ever since. Patch tests were performed with hydrocortisone acetate ointment *Z* which produced a severe weeping erythema. Patch tests with the base and neomycin were negative.

Case 3.—A woman aged 68 developed eczema of the eyelids as an autosensitization reaction to long standing gravitational dermatitis. This healed on treatment in hospital. On her return home a month later, her eyelids again irritated and hydrocortisone acetate ointment *Z* with neomycin was prescribed. This produced a severe contact dermatitis which rapidly subsided on treatment with hydrocortisone acetate lotion *X*. Patch tests with neomycin ointment and the base were negative, but the patch test with hydrocortisone acetate ointment *Z* produced such a severe reaction that she had to take to her bed for three days. Understandably she declined the invitation to further patch testing !

Case 4.—A woman aged 62 had suffered from gravitational ulceration of the legs for thirty years, following deep thrombosis and for twelve years had had rheumatoid arthritis. She was admitted to hospital. As the ulcers healed she developed an eczematous eruption on the legs which was not due to applications to the ulcers. This was treated with hydrocortisone acetate ointment *W* which made the eruption much worse. Patch tests with this ointment produced severe reactions, while those to its base were negative. She was later treated with hydrocortisone acetate ointment of a different preparation *Y* combined with tetracycline, with great improvement and has continued to use this ointment ever since.

Case 5.—A schoolmistress aged 27 had had recurrent eczema of the eyelids and retroauricular areas for three years. In November 1957 she commenced using hydrocortisone acetate ointment *Z* and continued using this until five months later, when she complained that application of this ointment made her eyelids burn and the eczema worse. Patch tests to the ointment were positive, while those to the base were negative. She was then treated with hydrocortisone acetate ointment *X* and gradually recovered, until eight months after the onset of the contact dermatitis, she was discharged from the hospital out-patient department healed.

Investigations and Results.

In the case of the fourth patient the hydrocortisone acetate ointment *W* carried a different trade name, but it transpired that hydrocortisone acetates *W* and *Z* were made by the same process. That used in the manufacture of hydrocortisone acetates *X* and *Y* was entirely different.

A series of patch tests to various types of hydrocortisone preparations was carried out as the next stage in the investigation in patients 1, 2 and 5. In addition, the final solvent used during the manufacture of hydrocortisone acetate was used in a patch test.

Table I.—*Patch Tests, First Series.*

Substance.	Brand.	Reactions in Case 1.	Case 2.	Case 5.
Hydrocortisone acetate ointment	*Z*	+	+	+
Hydrocortisone acetate solution	*W*	+	+	Not tested.
Ointment base	..	—	—	—
Crystalline hydrocortisone acetate	*Z*	+	+	+
Hydrocortisone succinate lotion	*Z*	—	+	—
Crystalline hydrocortisone free alcohol	*Z*	—	Weak +	Weak +
Solvent	..	—	—	Not tested.
Hydrocortisone acetate lotion	*X*	—	—	,,
Hydrocortisone acetate ointment	*X*	—	—	,,

In the first two patients the patch tests to hydrocortisone acetate ointment *Z* were repeated on two subsequent occasions for demonstration purposes and remained positive. In Case 1 these repeated tests took place after his eczema had completely cleared, so that there was no possibility of a non-specific reaction in a patient with

active eczema. The weak reaction to crystalline hydrocortisone free alcohol and the absence of any reaction to hydrocortisone succinate in two of three patients suggested that hydrocortisone acetate itself was not the cause of the reactions, but that other chemicals which were more efficiently removed in production of the free alcohol and subsequent succinate forms could be responsible. Hydrocortisone preparations are not necessarily one hundred per cent pure; the British Pharmacopoeia allows a certain proportion of material other than hydrocortisone itself, so that a preparation may contain inactive steroids with physico-chemical properties very similar to those of hydrocortisone and possibly slight traces of other substances arising during production.

The next step necessary was a series of patch tests to the breakdown products in the manufacturing process and also the testing of highly purified hydrocortisone acetate. At this stage, patient 5 refused to submit to further patch tests. Fortunately patient 4 had become available in the meantime and for the co-operation and patience of these remaining three subjects I am most grateful.

In order to avoid any bias, the following thirteen materials for patch testing were supplied under code letters and the substances made known to me after the results were recorded:

TABLE II.—*Patch Tests, Second Series.*

Substance.	Reactions in Case 1.	Case 2.	Case 4.
Purified hydrocortisone acetate	—	—	—
Hydrocortisone acetate *X* in Base *Z*	—	—	—
Base *Z*	—	—	—
Hydrocortisone acetate *Z* 1%	++	++	++
0·5% Hydrocortisone alcohol	—	+	+
1% Hydrocortisone alcohol	—	+	+
0·25% 21-diol acetate	+	+	+
0·5% 21-diol acetate	+	+	+
1·0% 21-diol acetate	++	++	++
0·1% steroid intermediate	—	—	—
0·25% steroid intermediate	—	—	—
0·5% steroid intermediate	—	—	—
1·0% steroid intermediate	—	—	—

These tests indicated that the sensitizing substance was present at the stage of the hydrocortisone precursor 21-diol acetate.

One further series of patch tests was necessary to establish whether this was the 21-diol acetate itself, or an impurity. 21-diol acetate is present in the hydrocortisone acetate preparation in a concentration of about 1%. A further series of "blind" patch tests was performed on Case 4 and the code later revealed.

TABLE III.—*Patch Tests, Third Series.*

Substance.	Reactions in Case 4.	Three normal controls.
0·025% of a product obtained by concentration of the liquors from an ethyl acetate extraction of 21-diol acetate	+	Not tested.
1·0% of the residue after removal of above	+	
0·25% of a product obtained by concentration of the liquors from a methyl chloride extraction of 21-diol acetate	++	,,
1·0% of the residue after removal of above	++	,,
1·0% of specially purified 21-diol acetate	+	—

The reaction of this patient appeared to indicate that 21-diol acetate—to which she reacted even when the substance was specially purified—was the sensitizing

agent. The purified 21-diol acetate was later tested on three normal controls without reaction.

As a last series of patch tests, a specially prepared hydrocortisone acetate powder containing only 0·3% 21-diol acetate was used and caused a weakly positive reaction in Case 1 and positive reactions in Cases 2 and 4.

Discussion.

In the patients who reacted to brands *W* and *Z* of hydrocortisone acetate ointment the sensitizing agent was 21-diol acetate, the chemical precursor of hydrocortisone acetate. The last stage in the process of production of hydrocortisone acetate is conducted by catalysis, using osmium as the catalyst. This catalysis is not complete and about 1% of 21-diol acetate is present in the final product.

Hydrocortisone acetate ointment brands *W* and *Z* had been used on thousands of patients in the Sheffield area before these cases were discovered ; the very low incidence of reactions and the absence of reaction on normal controls proves that this substance is a sensitizing agent and not a primary irritant. The incidence of this sensitivity can also be kept in proportion by the fact that during the time these cases were discovered, one further case reacted to the ointment and was found to be sensitive to the wool fat contained in the base.

21-diol acetate is a precursor peculiar to the process involved in the production of these brands of hydrocortisone acetate, but it seems probable that other side products produced by other processes could be responsible for sensitization reactions.

The patient reported by Kooij reacted to patch tests with various brands of hydrocortisone acetate, all ointments containing neomycin, chloromycetin, achromycin, and a solution of hydrocortisone sodium succinate in water. Such polysensitivity in the presence of an active eczema suggests that some of these reactions may have been non-specific. If the sensitivity to hydrocortisone sodium succinate persisted it could have been due to by-products, as in the cases recorded here. Sensitivity to a pure hydrocortisone salt has yet to be proved.

Summary.

Five patients with eczema were found to react adversely to an ointment containing hydrocortisone acetate. Patch tests proved this reaction to be due to 21-diol acetate, a precursor of hydrocortisone acetate, small quantities of which were present in the final product.

I am grateful to Dr. Doris Fletcher for permission to quote Case 5. It is a pleasure to acknowledge the co-operation and work of the pharmaceutical companies concerned.

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CONTACT DERMATITIS FROM PARABEN

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THIS is a report of a patient with contact dermatitis from a proprietary ointment containing tetracycline, in whom the sensitivity was eventually traced to the "paraben" present in the preparation. This case was noteworthy from the first because the sensitivity appeared to be due to tetracycline and as the tetracyclines are regarded as having the lowest skin sensitization index, this would have been a rare finding.* When the sensitivity was in fact found to be due to paraben, the case assumed greater importance for two reasons. First, some reported cases of apparent tetracycline sensitivity may in reality have been due to paraben. Secondly, paraben is present in numerous drugs, foods and cosmetics in common use and awareness of this may uncover sensitivity reactions due to it but erroneously ascribed to other substances.

CASE REPORT.

A housewife aged 54 was seen in December 1959 with a seven years' history of varicose ulceration and stasis dematitis which had flared up and spread to the thighs and arms one month previously. She attributed the recent spread to the use of 3% Achromycin Ointment (Lederle). At about the same time she also used penicillin ointment with no ill effect.

Patch tests showed that she was sensitive to Achromycin Ointment (Lederle) which contains tetracycline hydrochloride 3%, methyl paraben 2·4% and propyl paraben 0·6%. However, she was patch tested with 3% tetracycline in soft paraffin and this gave a negative result. Paraben appeared to be the offending substance and more detailed patch tests were carried out (Table I). She was not given parabens orally.

TABLE I.—*Results of Patch Tests.*

Test substance	%	Result	
		At 48 hrs.	At 96 hrs.
Achromycin (Lederle)	3	++	++
Tetracycline	3	−	−
Propyl paraben	0·6	±	+
Propyl paraben	5	++	++
Propyl paraben + Methyl paraben	0·6 + 2·4	+	+
Methyl paraben	2·4	−	−
Methyl paraben	5	−	+
Penicillin ointment (20,000 units/g.)		−	−
Balsam of Peru	1	−	−

* Burstein (1950) and Calmettes *et al.* (1953) reported sensitivity to aureomycin (chlortetracycline) eye drops; Kooij (1959) found a positive patch test to 6% tetracycline and Vickers (1960) mentions a case of contact dermatitis from aureomycin. Sensitivity reactions due to systemic administration of aureomycin were noted by Peck and Feldman (1950), Shaffer *et al.* (1950), Bell and Rubitsky (1951) and Bedford (1951).

Discussion.

This patient was sensitive to 3% Achromycin Ointment (Lederle) which contains in addition to 3% tetracycline hydrochloride, methyl paraben 2·4% and propyl paraben 0·6%. Patch tests with propyl paraben were strongly positive. Weaker and delayed positive reactions were also obtained with methyl paraben, but patch testing with 3% tetracycline in soft paraffin gave a negative result. The concentration of the parabens in the proprietary preparation seemed unnecessarily high and this view was expressed to the drug manufacturing company, who are considering a modification of the formula.

Bonnevie (1940) reported the first case of sensitivity to ethyl paraben in the antifungal preparation " Mycocten " and in a larger unpublished series of cases (Hjorth, personal communication) he was able to show that hypersensitivity to Mycocten was almost invariably due to ethyl paraben and not to the salicylic acid which is also present in the preparation. Although paraben sensitivity appears to be uncommon in this country, it is possible that increased awareness of its sensitizing properties may lead to recognition of further cases in the future.

A Note on the Parabens.

The term " paraben " is a suffixed abbreviation used by the pharmaceutical profession in the United States of America and in the United States Pharmacopoeia, to denote esters of *p*-hydroxybenzoic acid. Thus, the methyl ester of *p*-hydroxybenzoic acid is referred to as methyl paraben and the propyl ester as propyl paraben. As pharmaceutical substances they are specified and described in the United States Pharmacopoeia and also in the British Pharmaceutical Codex.

The anti-microbial effect of alkyl esters of *p*-hydroxybenzoic acid and their suitability for use as preservatives of pharmaceuticals, cosmetics, foods, etc., were discovered by Sabalitschka (1924), who also showed (1949) the inhibitory effect of these esters on the growth of *Staphylococcus aureus* and on yeast fermentation. McVay and Sprunt (1951) suggested that, as these esters were suitable agents for combating monilia, they should be used as prophylactics in antibiotic therapy to prevent the development of moniliasis. Others confirmed the anti-monilial effect of parabens in the laboratory (Sabalitschka, 1955 ; Sabalitschka *et al.*, 1955).

These esters have become known throughout the world as effective preservatives under the registered trade mark of Nipa Esters (Nipa Laboratories Ltd., Treforest Industrial Estate, Pontypridd, Glam.). They are sold under such names as " Nipagin ", " Nipasol ", " Nipacombin ", " Nipasept ", etc., and are said to be quite harmless in the concentrations recommended for their use. They are obtainable as the free esters or as their sodium derivatives, and are used not only as preservatives but also as antiseptics and antioxidants. Nipagin-M and Nipasol-M (Nipa Laboratories Ltd.) are used as eye and nasal drops because of their antiseptic properties and also as preservatives for aqueous solutions, mixtures, syrups, milk preparations, skin creams and lotions, face powders, soaps, lipsticks, suntan preparations, hair lotions, etc. In these preparations they are used as additives in a concentration of the order of 0·01–0·1%.

Lomholt (1938) introduced these esters in the form of a solution, ointment and powder for the treatment of tinea pedis. He used ethyl paraben in alcoholic solution in a concentration of 5% in preparations known as " Mycocten " and " Amycen ".

In a study of toxic effects of esters of *p*-hydroxybenzoic acid on humans and in experimental animals, Sokol (1952) found that these substances were remarkably safe. Patch tests carried out on 50 human subjects showed no evidence of allergic sensitivity. Four alkyl esters of *p*-hydroxybenzoic acid in propylene glycol prepared in concentrations of 5, 7, 10, 12 and 15% were applied to the backs of 50 human subjects for a period of five days. No irritant effect at all was noted at the following concentrations :

	%
Methyl paraben . . .	5
Ethyl ,, . . .	7
Propyl ,, . . .	12
Butyl ,, . . .	5

I wish to thank Dr. D. I. Williams for permission to publish this case and Dr. C. D. Calnan for drawing my attention to parabens. I should also like to thank Dr. R. Williams of Nipa Laboratories Ltd. for his help.

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CONTACT DERMATITIS DUE TO GOLD.

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THE PRECIOUS metals gold, silver and platinum have rarely been proved to be the cause of contact dermatitis, although dermatitis beneath a wedding ring is quite commonly seen. It is mainly due to the irritant effects of soaps and detergents and even if the ring itself is considered to be the cause, reactions to base metals combined with the gold are usually suspected. But very occasionally, true contact sensitivity to gold can occur as is illustrated by the following case.

CASE REPORT.

A married woman aged 20 years was first seen with a small patch of chronic discoid lupus erythematosus on the scalp. No treatment was considered necessary and at no time did she receive gold injections. When seen again a year later, the scalp lesion was inactive but she now complained of an irritable eruption underneath her 22-carat gold wedding ring. The rash had started a year previously, three months after her marriage. Examination showed a vesicular eruption underneath her wedding ring and on her ear lobes where she wore gold sleepers. Patch tests carried out on her forearm with the ring and the sleeper were positive and 0·5% sodium aurothiomalate solution applied as a patch test produced a violent reaction which took a fortnight to settle down. Further patch tests to gold leaf were positive and to pure strip silver and platinum, negative. The eruption on the ears settled rapidly, after the sleepers were removed, but she still complained of some itching of the ring finger two months later.

DISCUSSION.

Gold salts given parenterally frequently cause dermatitis, but metallic gold and even its salts have rarely been reported as a cause of contact sensitivity, though Schwartz *et al.* (1957) mention the occurrence of dermatitis in photographers due to gold chloride.

Forster and Dickey (1949) described a patient who developed a seropurulent discharge and eczematous contact-type dermatitis of the lids and adjacent skin five years after the enucleation of an eye and the implantation of a 14 carat gold ball containing 60% fine gold, 35% copper and 5% silver and tin. Positive patch tests were obtained to copper sulphate, gold sodium thiosulphate, the gold ball and gold leaf but not to silver, copper and tin leaf.

Gaul (1954) patch tested 100 patients with various dermatoses due to metals and their salts and noted a patient with dermatitis underneath a gold ring who was sensitive to 22 carat gold and 1% solution of gold sodium thiosulphate.

Gaul (1958) also showed that common salt can act with metals as a primary irritant. He described the case of a twelve year old girl who showed no skin reaction to 24 carat gold, but developed a follicular erythema 48 hours after the application of a patch test of gold and common salt, which persisted for several days.

Metallic gold is not a primary irritant. Gaul (1954) obtained no positive patch test to 24 carat gold in eight normal individuals. Metallic salts usually give a stronger reaction than the parent metal (Gaul, 1954) and as described, my patient produced a much more vigorous response to sodium aurothiomalate than to leaf gold. The case was neither traumatic in origin, as the patch test to leaf gold was positive, nor was it due to primary irritation. It is therefore thought to represent a true epidermal sensitivity to gold.

Summary.

A case is described of contact dermatitis due to allergic sensitivity to gold.

I would like to thank Dr. I. B. Sneddon for permission to publish this case, and for helpful criticism, in which Dr. R. E. Church joined.

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THE EFFECT OF ASPIRIN IN CHRONIC URTICARIA.

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A FEW individuals react to aspirin by developing urticarial weals and giant swellings which may represent true allergy to aspirin. However, in a series of patients with chronic urticaria from various causes, some developed an obvious increase in the weals and swellings after taking aspirin and these exacerbations of existing urticaria are difficult to explain on an allergic basis.

Under the heading of chronic urticaria I include patients in whom the condition has been present for at least six weeks. Papular urticaria of childhood, cholinergic, cold or actinic urticaria and dermographism are not included. Giant urticaria (angio-neurotic oedema) commonly occurs in patients with dermal weals, but cases with giant swellings alone are excluded.

During the past three years, seventy patients with chronic urticaria have been studied with regard to the effect of aspirin. Twenty of these gave a history of exacerbations of weals and giant swellings shortly after taking aspirin in various forms. The exacerbations settled down in a few days to the degree of urticaria prior to taking the aspirin. Test doses of aspirin varying from 5–15 grains were then given to the patients and sixteen out of the twenty showed an obvious increase in the eruption. Six more cases without such a history also reacted in this way to the test doses. The patients were next tested with sodium salicylate which gave the same results as aspirin.

The effect of aspirin and sodium salicylate appeared to be quantitative. It was greater if larger doses were used. This was sometimes apparent clinically when a patient with chronic urticaria had taken an occasional aspirin without any obvious trouble, but at another time took much more, and had a severe exacerbation. The effect was also more noticeable during phases when the underlying urticarial tendency was greater. Thus in a patient with severe wealing from chronic urticaria, a small dose of aspirin such as $2\frac{1}{2}$ grains produced a severe exacerbation, whereas in the same patient at a later stage, when the wealing tendency was less, as much as 15 grains hardly showed any effect.

DISCUSSION

The most likely explanation of this effect of salicylates seems to be that they act as histamine liberators. In a case of urticaria pigmentosa, Hamrin (1957) showed that attacks of flushing occurred when salicylates were given and suggested that this was due to release of histamine. Other drugs may have a similar effect. For example, it has long been known that morphia and its

derivatives should be avoided in the treatment of urticaria, as the weals may be increased and morphia is a known histamine liberator (Feldberg and Paton, 1951). The apparent quantitative effect of salicylates would fit in with such an explanation. On the other hand it is not easy to explain why the phenomenon is only present in twenty-two out of seventy patients.

Another possible explanation is linked with the fact that some cases of chronic urticaria appear to start as acute attacks associated with allergy to a drug or food. Thus in ten of the seventy patients mentioned, penicillin in five, anti-tetanus serum in two, crab, tinned fish and an attack of gastro-enteritis in one instance each, appeared to cause acute attacks of urticaria which then continued for months in a state not differing in any way from the other cases of chronic urticaria. Furthermore, two of the ten patients had histories of previous phases of urticaria unrelated to the drug or food in question. I have no real explanation for such acute attacks progressing to the chronic state, but it would seem possible that these patients had a latent constitutional tendency to urticaria which was triggered off by the acute attack. It might be argued that the exacerbations by aspirin in chronic urticaria are due to a similar mechanism, and that there is a true allergy to aspirin in these cases, occurring in patients with a constitutional tendency to urticaria. On the other hand, the phenomenon was noticed in twenty-two of the seventy patients and it seems unlikely that such a high proportion of a selected group of patients would be allergic to aspirin.

Whatever the explanation, patients with chronic urticaria should be advised to avoid salicylates in any form.

Summary.

Twenty-two out of seventy patients with chronic urticaria developed exacerbations of weals and giant swellings after the administration of aspirin or sodium salicylate.

The effect was more obvious when large doses were used and at times when the wealing tendency was greater.

It is likely that salicylates act as histamine liberators in producing this effect.

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TOPICAL TRIAMCINOLONE IN ECZEMA.

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The local application of hydrocortisone has been recognized as effective in the control of many dermatoses since it was introduced by Sulzberger and Witten (1952). It was to be expected that some of the newer steroids might have greater anti-inflammatory properties. Inman (1959) found topical prednisolone as effective as hydrocortisone and advocated its use because it was cheaper, but Frank and Stritzler (1955) and Smith (1956) reported that it was less effective. We also have found topical prednisolone disappointing but one of its analogues, triamcinolone acetonide (9-alpha-fluoro 16-alpha-hydroxyl prednisolone acetonide) seemed to us to have a considerably greater anti-inflammatory action than hydrocortisone. Three American reports claimed triamcinolone acetonide to be more effective than hydrocortisone (Robinson, 1958 ; Smith, Zawizsa and Blank, 1958 ; Epstein, 1959).

This paper presents the results of the first comparative trial in this country of topical applications of triamcinolone acetonide and hydrocortisone.

Investigation.

Only patients with symmetrical eruptions on the limbs were admitted to the trial and all were suffering from a type of dermatosis that might be expected to respond to the topical application of a steroid. The two steroids were supplied in ointment form, the base being identical and the tubes labelled *X* and *W*. Hydrocortisone was used in 1% and triamcinolone in 0·1% concentration. The identity of the preparations was known only to the manufacturers until after the trial had been completed. Each patient was supplied with a 15 g. tube of *X* and an apparently identical tube of *W*, with instructions to apply a small amount of ointment twice daily, *X* to one limb or lesion and *W* to the opposite side. The side to be treated with *X* was taken at random. When all four limbs were involved, *X* was applied to one upper limb and the opposite lower limb, and *W* to the remaining limbs, thus two paired results could be obtained on one patient.

The patients were reviewed from three to seven days after entering the trial and for greater accuracy two observers usually saw each patient. It soon became obvious that *X* was far superior to *W* and precautions were taken so that the observer reading the result was not aware of the side of application of *X*. When the first assessment was made it was often found that the side treated with *X* had completely resolved. If this were not so, the patient was instructed to reverse the sites of application and was reviewed in a further three to seven days. This technique again increased the number of paired comparisons available.

Results.

Sixty patients were admitted to the trial and of these three were rejected because they failed to comply with the conditions imposed (one found *X* so much better than *W* that she used it on both sides after 48 hours). The results are shown in Table I. Assessment of the results of treatment was

Table I.—*Results of Trial.*

Diagnosis.	Number of patients.	Pairs.	*X* better than *W*.	*W* better than *X*.	No difference.
Atopic eczema	33	49	46	3	—
Contact eczema	9	22	21	—	1
Discoid eczema	7	11	11	—	—
Seborrhoeic eczema	5	12	12	—	—
Senile eczema	2	4	4	—	—
Lichen simplex	1	2	2	—	—
Total	57	100	96	3	1

X = Triamcinolone acetonide, 0·1%.
W = Hydrocortisone, 1%.

easy, as there was a clear-cut difference between the two sides in almost all patients. The difference was most striking in patients suffering from atopic eczema and least in those with seborrhoeic eczema. Many of the patients with the former had used topical hydrocortisone in the past and were able to pick out *X* as the most potent agent they had experienced. It is interesting to note, however, that both patients in whom hydrocortisone was more effective were suffering from atopic eczema. In a small group of patients followed to complete clearance of the lesions, it was found that this was achieved 25% more quickly with triamcinolone.

Discussion.

The results confirm the American reports that triamcinolone is a more effective topical steroid than hydrocortisone. The present trial was restricted to those types of dermatosis that might be expected to respond to a topical steroid and this explains the high percentage of successful results. In only 3% was hydrocortisone found better than triamcinolone and this compares well with the figure of 5% quoted by Epstein (1959). It is our impression that some of the more difficult cases are controlled by 0·1% triamcinolone acetonide when 1% hydrocortisone has failed. This may be due to development of partial resistance to hydrocortisone following its prolonged use : thus a new steroid will give an apparently enhanced effect. Only time will show if this is the real answer. Even if so, triamcinolone offers an alternative in these more difficult cases.

The patients who derived the greatest benefit were those suffering from

atopic eczema, whilst patients suffering from seborrhoeic eczema derived the least (cf. Epstein, 1959). Triamcinolone acetonide is at present 25% more expensive than hydrocortisone and it seems reasonable to use it as a second line of therapy in patients where the response to the latter is either incomplete or slow.

Summary.

The results are presented of a double blind paired comparative trial of ointments containing 1% hydrocortisone and 0·1% triamcinolone acetonide. The latter is shown to exert a more powerful and more rapid anti-inflammatory effect in patients with various forms of eczema.

We wish to thank Dr. I. B. Sneddon and Dr. R. E. Church for permission to treat their patients and for much helpful criticism and advice. Messrs. E. R. Squibb Ltd. kindly donated generous supplies of 0·1% triamcinolone acetonide (Adcortyl A) and 1% hydrocortisone in a similar greasy base.

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THE TREATMENT OF LICHEN PLANUS WITH DIPASIC.

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Lichen planus is frequently difficult to treat successfully. Some cases will undoubtedly clear rapidly with arsenic or perchloride of mercury by mouth, or even with local antipruritic preparations : probably such cases would clear spontaneously. Nevertheless, many are most resistant to treatment, especially the hypertrophic variety, which may persist for over 20 years without showing any improvement. Treatment of the disease is empirical and in addition to the preparations mentioned, many local applications, local x-ray therapy to hypertrophic lesions, and bizarre forms of treatment, such as spinal irradiation and lumbar puncture, have met with success from time to time. Recently A.C.T.H. and corticosteroids have proved successful and Kristjansen and Reymann (1955) claimed 50% cure in 14 days with a 50% relapse rate in those cured. Hypertrophic lichen planus was not affected by A.C.T.H. Apart from in the exceptionally severe generalized type, it seems unjustifiable to use steroid therapy in this disease. The present report concerns the effect of Dipasic (the *p*-aminosalicylic acid salt of isonicotinic acid hydrazide) on lichen planus.

Materials and Dosage.

Initially a group of thirty patients was treated. Alternate cases were given placebo tablets identical in appearance to Dipasic. A further thirty patients were subsequently treated with Dipasic. This latter group included the cases which had shown no response to the placebo tablets. The dosage and duration of treatment was arbitrarily fixed at 600 mg. daily for 6 weeks and 300 mg. daily for a further 6 weeks. Local treatment, apart from talcum powder, was avoided entirely. The dose of placebo tablets was similar.

Results.

The results are shown in Table I. All the cases were followed up for at least 6 months and some for over 2 years. Those cases in which marked improvement occurred will almost certainly recover completely. Of the forty-one cases adequately observed, which were treated with Dipasic, thirty-two had a very good response to treatment, although only five out of fourteen controls showed a similar response. Four of the treated cases and eight of the controls showed no response whatever. Four of the latter eight cases (after a period of at least 3 months had elapsed following the administrations of placebo

TABLE I.—*The Overall Results.*

Treatment.	Number of cases. Treated.	Defaulted.	Followed up.	Results. Cured.	Greatly improved.	Improved.	No effect.
Dipasic	47	6	41	26	6	5	4
Controls	15	1	14	5	—	1	8

tablets) showed an excellent response to subsequent treatment with Dipasic. One of the eight control failures cleared up after injections of cytamen (Vit. B_{12}) by her own doctor.

A more detailed analysis of the cases treated with Dipasic, shown in Table II, indicates that the acute generalized type and the more local chronic type of lichen planus, such as occurs on the wrists and forearms, respond more readily to Dipasic than the hypertrophic variety. Nevertheless, some cases of the latter respond. The one which was cured had been present, despite all other treatment, for 25 years. Moreover, three of the cases in the other groups had hypertrophic lesions on the legs which responded equally as well as the papular lesions elsewhere. Mucous lesions did not show quite such a good response. Out of eleven followed up cases with mucous lesions the latter cleared in six, improved in one and in four showed no change. In two of the latter, the skin eruption cleared with Dipasic. Six of the forty-one followed up cases relapsed after apparent cure. One failed to respond to liq. hydrarg. perchlor., but this case along with the other five cleared when Dipasic was re-administered.

COMMENT.

The choice of Dipasic as a therapeutic remedy in lichen planus was fortuitous. It was originally suggested by my colleague, Dr. A. C. Dewar, who had observed a strongly positive Mantoux reaction in a case of lichen planus. There is, however, no evidence to suggest that tuberculosis plays any part in the aetiology

TABLE II.—*More Detailed Results.*

Type of case.	Number.	Duration.	Previous failures.	Results. Cured.	Greatly Improved.	Improved.	No effect.
Local lichen planus of papular type	4	Over 1 year	4	1	1	—	2
	4	6–12 months	2	2	2	—	—
	14	Less than 6 months	5	11	1	2	—
Widespread or generalized lichen planus	3	Over 1 year	3	2	—	1	—
	5	6–12 months	3	4	1	—	—
	5	Less than 6 months	1	5	—	—	—
Hypertrophic lichen planus	4	Over 1 year	4	1	1	1	1
	1	6–12 months	1	—	—	1	—
	1	Less than 6 months	1	—	—	—	1

of this disease. The mechanism of action of Dipasic in lichen planus is unknown and it is not claimed as a specific treatment for this disease.

A proportion of cases undoubtedly clear spontaneously, as can be seen from the control series. Nevertheless there is no doubt from the results that we have here a valuable remedy for this often intractable disorder. In the present unselected series of cases it has given almost 80% success. This compares favourably with that reported for A.C.T.H. Moreover, some of the cases have been of very long standing. Dipasic has the added advantage over arsenic and mercury of being relatively non-toxic. No patients complained of any upset at all and no deleterious effects were observed. The most remarkable feature of the results was the rapidity with which itching was relieved. This usually occurred within the first 2 or 3 weeks. It may be that the arbitrary dose given was greater than necessary but only further experience can determine this.

Summary.

A series of forty-one cases of lichen planus has been treated with Dipasic, the *p*-aminosalicylic acid salt of isonicotinic acid hydrazide. Thirty-two showed an excellent response compared with five out of fourteen control cases. The hypertrophic variety of lichen planus responded less readily than other types. No toxic effects were observed. The mechanism of action of the drug in lichen planus is not known.

I wish to thank Messrs. Bengué and Co. Ltd. for a generous supply of Dipasic and identical dummy tablets. I am also indebted to Dr. G. Harvey for permission to publish these results.

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THE TREATMENT OF ONYCHOMYCOSIS WITH GRISEOFULVIN.

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Onychomycosis, particularly when due to *Trichophyton rubrum*, has hitherto been regarded as almost incurable. Many considered that surgical avulsion of the nails offered the only chance of cure but even then relapse was frequent. The advent of griseofulvin was therefore most welcome. Numerous papers have now been published confirming the preliminary observations of Williams *et al.* (1958) that oral griseofulvin is an effective treatment for many superficial mycoses. Reports indicate that nail infections respond favourably though few cures have yet been claimed and the best treatment schedule is still undetermined. Blank *et al.* (1959) treated 200 patients, 76 with nail involvement. They found that infected finger nails became normal in 4 months and toe nails in over 6 months. Harvey *et al.* (1960) treated patients for 8 to 29 weeks and claimed cure in 8 out of 20 with nail infections ; 9 others improved. Our own early experiences have been recorded elsewhere (Barlow *et al.*, 1959). After short courses of griseofulvin, we noted considerable improvement in the appearance of finger nails and eradicated the infection in a few. The response of toe nails was less satisfactory. Many failed to improve and none cleared completely. We concluded, that to achieve a cure, it would be necessary to give griseofulvin, continuously or intermittently, over the whole of the period required for complete regrowth of the nail—possibly over a year in the case of toe nails. We suggested that removal of the nails might be advisable to shorten the period required for treatment. The present paper records experiences with a group so treated and compares a second group of patients treated conservatively.

Investigation.

Since May 1959, all patients presenting with onychomycosis have been treated with griseofulvin. All were advised that treatment might have to be continued for several months and that removal of the affected nails would probably hasten cure. From May to November 1959, 18 patients (6 male, 12 female) agreed to have their nails avulsed. One man subsequently ceased attending but the remaining 17 were under observation for at least five months (Group 1) : 16 patients (12 male, 4 female) decided against operation and were treated with griseofulvin and local applications (Group 2). The minimum period of observation in this group was six months.

Group 1.—Details of age, sex, duration of infection, nails affected and the presence or absence of skin infection, are given in Table I. In every case the fungus was identified before starting treatment. Scrapings were examined in 10% potash and cultures were made on Sabouraud's glucose and preservation media, each containing 40 units of streptomycin and 20 units of penicillin per ml. The infecting fungus was *T. rubrum* in fourteen patients, *T. mentagrophytes* in two (8, 10). In one patient (17) *T. mentagrophytes* was cultured from nail scrapings, *T. rubrum* from interdigital scales. Further

TABLE I.—*Patients Treated with Griseofulvin and Subjected to Nail Avulsion (Group 1).*

No.	Sex.	Age (yrs.).	Duration of nail infection (yrs.).	Skin involvement.	Toe nails removed.	Finger nails removed.	Duration of post-operative therapy with griseofulvin (months).	Period of observation after stopping griseofulvin (months).	Complication.	Result.
1	M.	46	18	−	+		11	Treatment continues	Re-infection *T. rubrum*	Failure.
2	,,	49	12	+	+	+	5	5	*C. albicans*	Cure.
3	F.	29	15	+	+	+	5	5	,, ,,	,,
4	,,	53	3	+	+		5	6	,, ,,	,,
5	,,	43	12	+	+		5	4	None	,,
6	,,	14	?	−	+		3	5	Pityriasis rubra pilaris	Infection cleared.
7	,,	59	8	+	+		4	3	None	Cure.
8	M.	51	4	+	+		3	5	*C. albicans*	,,
9	F.	45	10	+	+		5	4	Smooth skin relapse	,,
10	,,	42	1	−	+	−	5	3	*C. albicans*	Infected (*C. albicans*).
11	,,	32	7	+	+	+	2	5	,, ,,	Cure.
12	,,	39	9	+	+	+	3	3	None	,,
13	,,	46	?	+	+		3	3	,,	,,
14	M.	31	15	+	+	−	3	3	,,	,,
15	F.	19	4	+	+	−	2	3	*C. albicans*	Infected (*C. albicans*).
16	M.	43	14	+	+	+	2	3	*C. albicans*	Cure.
17	F.	51	2	+	+	−	2	3	None	,,

examinations were carried out two to four months after avulsion (by which time new nail formation was usually well advanced) and thereafter at monthly intervals. Local treatment was always stopped a few days before taking samples to reduce interference with culture.

Two of these patients (13, 14) received griseofulvin 0·25 g. q.i.d. for five months before deciding to have their nails removed. Three others (6, 7, 9) received pre-operative treatment for three months. The remaining 12 were given griseofulvin 0·5 g. q.i.d. for a few days before nail avulsion, the dosage then being reduced to 0·25 g. q.i.d.

Removal under local anaesthesia was usual when only two or three nails were affected ; for multiple nail infection general anaesthesia was preferred. Whitfield's ointment was used as a local application in almost all cases. Post-operative discomfort was slight and no immediate complications were noted. Finger nails reappeared within two weeks and growth was complete in three to four months. Toe nails took up to six months to regrow completely. In four patients treatment was stopped two months after nail removal ; in the remainder it was continued until two successive negative cultures were obtained.

Group 2.—Details of this group are recorded in Table II. All were infected with *T. rubrum*. Involved sites were checked at monthly intervals and treatment was continued till two successive cultures were negative. The dosage of griseofulvin was 0·25 g. q.i.d., and Whitfield's ointment was again used as the local application.

Results

Group 1 *:* 17 patients (see Table I).—Those with skin involvement reported less itching within a few days, glabrous skin lesions disappeared in about two weeks and palms and soles were clear clinically in six to eight weeks. In some, maceration persisted between the toes though microscopical examination and culture became negative. One patient (9) relapsed on the leg two months after stopping treatment but responded to a further month's course of griseofulvin and her nails remained clear. She was the only one in whom the skin became re-infected. Finger nails always grew out normally following avulsion. The toe nails grew out normally in seven patients. In eight, they became infected with *Candida albicans*. This showed itself as a yellowish discoloration and thickening of the terminal portion of the nail. By applying nystatin ointment and trimming the nail it was possible to clear the candida infection in six patients but in two the terminal dystrophy persists.

In one case (1), all the toe nails were removed but four grew back in a dystrophic manner and remained infected with *T. rubrum* despite continuing griseofulvin. It was suspected that the fungus had become resistant but *in vitro* studies did not support this idea. Griseofulvin in 50% alcohol, added to Sabouraud's broth medium to produce a concentration of 5 μg./ml., completely inhibited growth of the patient's fungus whereas no inhibition was noted when the solvent was used alone. The remaining patient was of particular interest. This girl had pityriasis rubra pilaris and though *T. rubrum* was found in all her toe nails it was difficult to know how much the infection contributed to the nail changes. No fungus could be found on the palms and soles which had the typical appearance of pityriasis rubra pilaris and the finger nails were normal. It was no longer possible to find the fungus in her toe nails after

TABLE II.—*Patients Treated with Griseofulvin, Nails not Avulsed (Group 2).*

No.	Sex.	Age (yrs.).	Duration of nail infection (yrs.).	Skin involvement.	Toe nails affected.	Finger nails affected.	Duration of treatment (months).	Period of observation after stopping griseofulvin (months).	Complications.	Result.
1	F.	33	12	+	+	−	12	Treatment continues	None	Improved.
2	,,	6	1	+	+	−	6	4	,,	Cure.
3	M.	43	5	+	+	+	12	Treatment continues	Smooth skin relapse	Improved.*
4	,,	54	4	+	+	+	6	4	None	Cure.
5	,,	50	15	+	+	+	11	Treatment continues	*C. albicans*	Improved.*
6	,,	26	7	+	+	+	8	0	None	Cure.
7	,,	72	20	+	+	−	9	Treatment continues	,,	No change.
8	F.	25	11	+	+	−	5	5	Relapse, skin and nails	Still infected (*T. rubrum*).
9	M.	62	20	+	+	+	7	Treatment continues	*C. albicans*	Improved.*
10	,,	47	4	-	+	−	5	3	None	Cure.
11	,,	14	3	+	+	−	6	2	Relapse, skin and nails	*C. albicans*, nails, *T. rubrum*, skin.
12	,,	66	?	+	+	+	10	Treatment continues	*C. albicans*	Improved.
13	,,	42	7	-	+	−	7	4	None	Cure.
14	,,	40	6	-	+	−	9	0	,,	,,
15	F.	33	9	-	+	+	6	1	,,	,,
16	M.	26	3	+	-	+	6	0	,,	,,

* Finger nails have cleared. Result indicated refers to toe nails.

treatment but they regrew in a dystrophic manner and the clinical appearance was unchanged.

Group 2 : 16 patients (see Table II).—Skin infections responded initially as in Group 1. One patient (3) sustained a relapse after 9 months' treatment when *T. rubrum* was again isolated from the outer toe clefts and clinical and mycological evidence of infection is still present at these sites after a further 3 months' treatment. In two other patients (8, 11), re-infection of the skin was noted two months after stopping treatment. The skin remained clear in all other cases. Eight of the group had infected finger nails. In every case they grew out normally in three to six months. Fifteen patients had infected toe nails. The toe nails cleared in nine after five to nine months but became re-infected with *T. rubrum* in one case (8) two months after stopping treatment. Clinical relapse also occurred in another patient (11) two months after apparent cure. In this case, *Candida albicans* was isolated from the nails and, as already noted, *T. rubrum* from the toe clefts.

The six patients with persisting toe nail infection have shown a variable response after six to twelve months' treatment. One (17) shows no improvement after nine months, two others improved initially but the condition of their nails has now been static for several months and avulsion will probably be required. In three patients slow improvement continues but at present rates complete clearance of the nails may take over eighteen months. Both *C. albicans* and *T. rubrum* have been isolated from the nails of these three patients.

Toxic effects.—A few patients complained of headache when starting griseofulvin but it was never severe. Slight depression of the leucocyte count was occasionally noted a few days after the commencement of treatment but no counts lower than 4,000 per cu.mm. were obtained. Counts remained within the normal range after nine months' treatment and we no longer feel it necessary to carry out routine blood tests but warn patients to report symptoms.

Discussion.

The precise mode of action of griseofulvin remains uncertain though it is known to be fungistatic and not fungicidal. After ingestion and absorption the drug is deposited in the keratinized structures which are thereby made resistant to fungal invasion. As treatment continues, the infected layers of smooth skin are cast off in the normal way. A resistant band of keratin extends distally in the nail plate, the infected portions being pushed outwards and eventually cut away. A short course of griseofulvin is rarely effective in clearing nail infections. The soft keratin of the periungual skin, rendered resistant to fungal infection by griseofulvin, is shed before the diseased part of the nail grows out. Reinfection of the skin can then take place and the proximal parts of the nail may be attacked by fungus travelling round the resistant portion of nail plate. Local fungicides do not prevent this spread. Thus cure is unlikely unless

treatment is continued till all signs of nail infection have disappeared. Less time is required to clear the infection if diseased nails are removed ; the advantage of the shorter period of treatment are pointed out below. Nail avulsion also renders cure more likely, judging by the results of this trial, though more prolonged observation will be required to confirm this view (see Table III). Distinction is also necessary between toe and finger nails. The latter invariably clear within six months of starting griseofulvin and avulsion offers little advantage. Toe nails present a more difficult problem. They respond very variably, and from the evidence available in this series it is impossible to say whether such factors as age, duration of infection, skin involvement or degree of nail dystrophy are of any value in predicting the outcome of treatment. The worst result was obtained in the oldest patient—possibly because the rate of nail growth falls off in old age (Le Gros Clark and Buxton, 1938). The variable

TABLE III.—*Comparison of Results in Groups* 1 *and* 2, *Toe Nail Infections.*

	Number of patients with toe nail infections.	Still infected *T. rubrum.*	Infected *C. albicans.*	Cleared of infection.	Average duration of treatment in patients cleared of infection (months).†
Group 1 (avulsion)	17	1	2	14	3·6
Group 2 (no avulsion)	15	7	4*	7	6·7

* This figure includes 3 patients whose toe nails are also infected with *T. rubrum.*

† Refers to post-operative treatment only : 5 patients received griseofulvin for 3–5 months before avulsion but it is unlikely that this influenced the final result.

response in other patients and indeed, in different nails of the one patient, may be partly due to differences in rates of nail growth. It is also possible that local environmental conditions influence the metabolism of griseofulvin and on occasions reduce its efficacy. There seems to be no other explanation for the failure of treatment in the first patient of Group 1.

Some whose toe nails were avulsed would almost certainly have been cured by the conservative regime. However, since it is difficult to foretell the likely response of any individual it seems justifiable at the outset to recommend toe nail avulsion as offering the best chance of cure. Some who find the procedure repugnant, may be treated conservatively for a few months. Those responding poorly can then be subjected to the operation. Following avulsion it is unnecessary to continue griseofulvin until nail growth is complete. In this trial, those receiving the drug for two months post-operatively, fared just as well as those receiving it for five. The shorter period of treatment is obviously cheaper and decreases the risk of long-term toxic effects—which has yet to be assessed. It is also desirable if fungal resistance, already demonstrated *in vitro* by Robinson *et al.* (1960), becomes a clinical problem. Cowan (1960)

has suggested that intermittent treatment with griseofulvin may offer similar advantages.

Secondary infection with *Candida albicans* was common in this series, particularly in those whose nails were avulsed. Fortunately, topical nystatin controlled this complication in most cases. The problem of reinfection with trichophyta can only be assessed by long term studies. Sterilization of fomites would seem desirable. It is likely, nevertheless, that certain types of skin will remain fertile soil for fungi and that the need for griseofulvin will continue.

Summary.

The results of griseofulvin treatment in 33 cases of onychomycosis are presented.

Infected nails were removed in 17 patients; all had infected toe nails. Five also had infected finger nails. Toe nails are now clear of infection in 14, remain infected with *T. rubrum* in 1 and are infected with *C. albicans* in 2. Finger nails are all normal.

During the same period, 16 patients were treated with griseofulvin and topical applications alone : 15 had infected toe nails and of these 7 are now clear of infection, 4 are still infected with *T. rubrum*, 1 is infected with *C. albicans* and 3 are infected with both fungi. Eight patients had infected finger nails. These have become normal in every case.

It is concluded that nail avulsion is unnecessary in finger nail infections but offers a quicker and more likely cure in toe nail infections.

I wish to thank Dr. F. F. Hellier and Dr. S. T. Anning who kindly allowed me to treat patients under their care, Dr. C. J. La Touche for his invaluable help with the mycological studies and Mr. M. Ellis, Surgeon in Charge, Receiving Room, who allowed me to avulse nails in his Department.

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A MEATAL TROWEL*

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In spite of the widespread use of antibiotic and hydrocortisone fluids and powders, the need persists for the application of ointments and particularly of zinc pastes, for dermatological conditions of the external auditory canal, especially for lesions of the outer orifice of the external meatus.

Fig. 1.

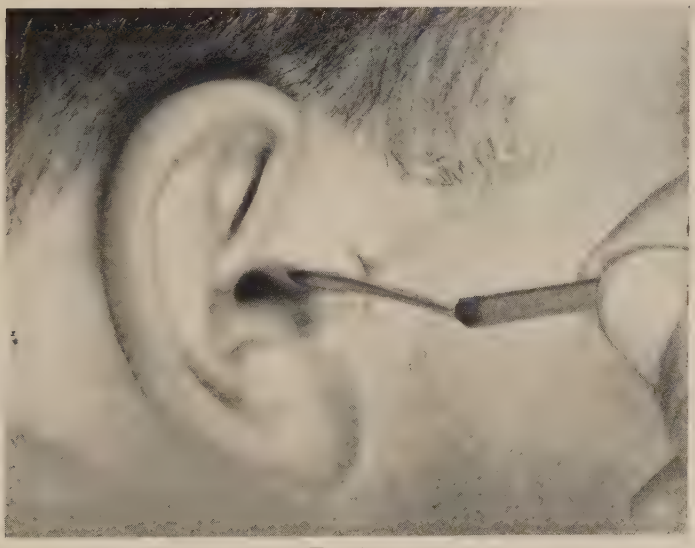

Fig. 2.

The application of ointments or pastes to this area is notoriously difficult ; I have found it much facilitated by a small applicator which for some years past I have used for this purpose (Fig. 1). For want of a better name, I have called it a Meatal Trowel. The use of the instrument is best explained by the illustration (Fig. 2) ; its rounded circumference makes injury of the external canal unlikely.

The instrument is now being made by Messrs. Down Bros. (Meyer and Phelps).

* Demonstrated at the meeting of the Section of Dermatology of the Royal Society of Medicine on 19 March 1959.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. Hugh Gordon.

21 January 1960.

Cutaneous Vasculitis.—Dr. L. Forman.

A man aged 45. Storeman.

This patient was shown for me by Dr. Tatz in 1946 under the diagnosis of pityriasis lichenoides with necrotic lesions.

History.—Pleurisy (? pneumothorax) at age of 16, 21, and 26 years. ? Slight haemoptysis when aged 19. Four years ago, an episode of acute abdominal pain lasting several days.

Present condition.—Skin involved 1943 when aged 29. Crops of small flat papules which may involute with scale, or progress to haemorrhagic nodules up to 2 cm. across, over a period of two weeks, with haemorrhagic necrosis, separating away in a variable period of time, up to two months, to leave foveated scars.

Investigatins.—Skiagram of chest negative. No abnormal blood changes, no cryoglobulins, W.R. and Kahn negative, Mantoux (1946) 1/1000 slight positive.

Sections of early papules : show lymphocytes and plasma cells around small blood vessels of papillary and subpapillary layer, infiltration of these cells into the walls of the blood vessels which show fibrinous degeneration and escape of red blood cells.

Reference.

Tatz, K. (1946) *Proc. R. Soc. Med.*, **58**, 79.

Cutaneous Vasculitis.—Dr. L. Forman.

A man aged 28. Tug Skipper.

Family history.—Father had tuberculosis of lung.

History.—At age of 18 years developed Raynaud's phenomenon of the hands. Bilateral cervical sympathectomy. Excellent result for 3 years, but symptoms returned.

Present condition.—Complaining of recurrent necrotic lesions of the skin.

1958 : Isolated erythematous papule on left arm, which within 2 weeks had developed into a black necrotic area 1 cm. in diameter, healing with scarring.

1959 : Crop of twenty similar but smaller haemorrhagic necrotic papules on the trunk and limbs.

These have continued to appear, fewer in number and smaller in size.

Investigations.—Skiagram chest normal. Blood count and differential normal. Blood proteins and electrophoresis of serum normal, no cryoglobulins. E.S.R. (Westgren) 2 mm. 1 hr. Blood calcium 10·6 mg.% (normal).

Biopsy of early papular stage : polymorph and eosinophilic cells infiltrating superficial vessel walls, which show degeneration.

Dec. 1959 : Four teeth extracted.

Comment.—In both these patients the onset of the necrotic papules was at the same age, 28 and 29 years. The disease has been present for 16 years in the first case, and two in the second. Visceral symptoms in the first case have included repeated pleurisy, one haemoptysis and an attack of abdominal pain, possibly due to involvement of the mesentery.

The small vessels affected have been at the level of subpapillary and mid-cutis layer, and have shown some degeneration of the vessel wall and surrounds of lymphocytes, plasma cells, and in the second case, of a few eosinophils. In neither case has there been any evidence of tuberculosis, although a member of the patients family was a known tuberculous subject.

Dr. Brian Russell : One cannot ignore the possibility of these being tuberculides. The patient may not be overtly ill and it may not always be possible clinically to detect a focus of infection. I think that it is always worth carrying out a Mantoux test to ascertain whether the reaction is excessive in these patients.

Dr. Louis Forman : The first patient is still receiving a pension from the Army as a tuberculide. He has had a course of streptomycin and calciferol without influencing the appearance of the lichenoid and necrotic papules.

Leukoplakia of the Tongue and Cheeks ? Due to Arsenic ? ? Due to Peppermint.—Dr. L. Forman.

A married woman, aged 49.

History.—At the age of 17 was treated with medicine for approximately 8 weeks for St. Vitus' Dance. She has sucked peppermints for 16 years, particularly during the years 1943–48, when she took her ration of sweets, 2 oz., as peppermints (Mitcham mints).

Present condition.—Fourteen years of painful " ulceration " of tongue and mouth—no definite blisters have been recorded. Tongue warty, leukokeratotic with areas of atrophy. Plate smooth leukoplakia. Cheeks smooth leukoplakia particularly developed on inner aspect of the left cheek. Soles of feet dry and slightly hyperkeratotic. Heels show tiny keratomata. Pads of fingers show tiny localized keratomata.

Investigations.—Biopsy of scaling papule on right arm—localized acanthosis with keratinization and lymphocytic reaction beneath hard up against epithelium. Specimen of skin of the hypothenar eminence which showed slight hyperkeratosis, was sent to Dr. Aileen Scott for estimation of arsenical content in April 1959. She reported: " The wet weight was 0·5 g. and the total arsenic content was 1·2 μg./g. This was just above the upper limits of normal and we cannot say without doubt that she has had a large quantity of arsenic in her system. It does suggest, however, very strongly that this is a possibility."

Biopsy specimen from the tongue November 1959 : Dr. Aileen Scott reported : " The arsenic content was 1·8 μg./g."

W.R. and Kahn negative, Hb 64%, W.B.C. 3900 per cu.mm., normal differential count.

Comment.—In favour of the leukokeratosis of the tongue and leukoplakia of the cheeks being due to arsenic are the keratomata on the tips of the fingers, on the heels, and the solitary keratomatous lesion of the arm. Again, there is the finding of a significant amount of arsenic both in the palmar skin and the epithelium of the tongue.

Peppermint tablets can produce glossitis, and localized leukoplakia of the tongue, due to the irritant effect of peppermint or to the mechanical irritation of the tablet. Hyperkeratotic changes due to arsenic are commonly seen on the palms and soles possibly also localized by trauma.

Professor J. T. Ingram : I doubt the diagnosis of leukoplakia and suggest candidiasis. Has this been excluded? Does histology show atrophy and hyperkeratosis of epithelium?

Dr. Louis Forman : The only specimen removed was sent to Dr. Scott.

Dr. E. J. Moynahan : I am not quite clear as to whether it is concerned with sucking peppermint sweets or the ingestion of arsenic.

Dr. Louis Forman : Both.

The following cases have been published in *Proc. R. Soc. Med.*, **53**, 563.

Pemphigoid with Carcinoma of the Rectum.—Dr. L. Forman.

Pigmentation of the Nail Beds following the Administration of Plaquenil.—Dr. Anne Maguire (for Dr. Forman).

Granuloma Inguinale.—Dr. P. J. Hare.

The following cases were also shown:

Atopic Eczema, Ulcerative Colitis, Hepatosplenomegaly.—Dr. A. W. McKenzie (for Dr. Louis Forman).

(1) **Multiple Basal Celled Metaplasia and Bowen's Disease.** (2) **Urticaria Pigmentosa with Hepatosplenomegaly.**—Dr. Louis Forman.

Rhizopus Parasitica: Infection of Forearms.—Dr. E. J. Moynahan.

Urticaria Pigmentosa.—Dr. W. C. Marshall (for Dr. E. J. Moynahan).

Hyperkeratosis of Palms and Soles and "Periodontosis" (Papillon Lefevre's Syndrome).—Dr. E. J. Moynahan and Mr. W. G. Cross.

Brevicollis (Klippel-Feil Syndrome). Diastematomyelia. Satyr's Tail.—Dr. V. R. Bloom (for Dr. E. J. Moynahan).

Case for Diagnosis. ? Hamartoma.—Dr. E. Colin-Jones.

Pseudoxanthoma Elasticum.—Dr. D. Sharvill.

Cicatricial Alopecia : Lupoid Sycosis.—Dr. Peter Smith.

Dermatitis Traumatica of the Lips, Cured by Hypnosis.—Dr. M. J. Fenton.

18 February 1960.

Case for Diagnosis ? Mucinosis.—Dr. R. H. Marten.

A woman aged 20. Dental student.

History.—Four years, persistent lesions upper mid-chest. These, which have never completely cleared, become red and swollen after exposure to sunlight. Over the past few years occasional other lesions have occurred, but many of those on her back appeared while she was on holiday last summer. New lesions, some of which irritate, are still erupting on the back and arms. Individual papules may last up to several months and then either disappear completely or leave areas of depigmentation. The face, hands and lower legs have never been affected.

General health—excellent.

Past history—*nil* relevant.

Family history—*nil* relevant.

Clinical findings.—Scattered over the chest, back, shoulders and upper arms are a number of slightly raised, smooth, round or oval dermal papules measuring approximately 1 cm. in diameter. Each lesion has a pink centre and pale periphery, and some are surrounded by a white halo. There is no atrophy or epidermal change. Several small depigmented areas can be seen on the back and right shoulder at the sites of previous lesions. General examination—Normal. No evidence of thyroid disease.

Investigations.—Blood count—Hb 88%, W.B.C. 4300, Polys. 43, Lymphos. 38, Monos. 9, Eosinos. 9, Basos. 1%.

E.S.R.—1 mm./hr. L.E. cells—none seen. Plasma proteins—6·2 g./100 ml. Electrophoretic pattern—normal. Blood cholesterol—190 mg./100 ml. Chest skiagram—no abnormality seen in the heart and lungs. Urine—Normal.

Biopsy specimen from right shoulder showed a little keratotic plugging and occasional small foci of liquefaction degeneration of the basal cells. Throughout the dermis

collagen fibres are separated by basophilic material which stains with alcian blue and toluidine blue but fails to react with P.A.S. and mucicarmine. A patchy, though mainly perivascular, banal and predominantly lymphocytic cellular infiltrate is present in the dermis. There is some decrease in number of elastic fibres.

Comment.—I thought these lesions were unusual, but clinically one had to consider either lupus erythematosus or perhaps an early stage of macular atrophy.

However, there was no macular atrophy at the sites of previous lesions and the histology was not that of macular atrophy.

The striking histological change was the separation of the dermal collagen fibres by a basophilic material which stained with alcian blue and toluidine blue. Such a picture may be seen in myxoedema, pre-tibial myxoedema or lichen myxoedematosus. There was, however, no evidence of thyroid disease or pre-tibial lesions and the eruption did not conform with the clinical picture of lichen myxoedematosus.

Gold (1954) reported two patients with an unusual papular eruption associated with lupus erythematosus. The histology of these papules was similar to that in the present case, but the clinical appearances in his cases were different and both were suffering from systemic lupus erythematosus.

In my patient all investigations were normal and there was no evidence of discoid or systemic lupus erythematosus. Apart from the flare up of the lesions with sunlight there was little to suggest a diagnosis of lupus erythematosus in this case.

Reference.

Gold, S. C. (1954) *Brit. J. Derm.*, **66**, 429.

Lichen Sclerosus of the Penis.—Dr. Everall.

A man aged 40.

History.—Onset, April 1959, of irritating lesion of lichen sclerosus of the glans penis, associated with difficulty in micturition. At that time a small, atrophic, white, infiltrated area with a halo of erythema and telangiectasia was present on the glans and involved the meatus, accompanied by a serous crusted discharge. Meatal stenosis present. Rest of body clear. General examination negative.

Family history.—Negative.

Past illness.—Nil.

Investigations.—W.R. and Kahn negative. Skiagram of chest, peripheral blood count and E.S.R. normal. Histology showed gross acanthosis with homogenization of the dermal collagen with a band of round cell infiltration of the mid-dermis.

During the succeeding three months the lesion was treated with Ung. Triamcinolone Acetonide 0·1% locally and the meatus was dilated regularly weekly for the first month and then at two-weekly intervals. Over this period the lesion slowly resolved, leaving residual scarring and minimal residual meatal stenosis (Fig. 1).

Dr. H. Haber: At the Eleventh International Congress of Dermatology in Stockholm Dr. A. D. Harkness and I read a paper on lichen sclerosis et atrophicus of the external meatus under the title *Constricting Meatopathy of the Male Urethra* (1957). There were sixteen cases occurring in men of the middle-aged group with symptoms of urethral discharge associated with pain, frequency and difficulty in micturition. Discharge was clear and mucoid in character and under microscopic examination showed only a few organisms and no pus cells. The characteristic feature of the disease was the condition of the external urinary meatus which showed changes depending on the stage of disease, the objective changes never being observed by the patient. In the acute stage, the lips of the meatus were swollen, dead white, surrounded by an inflammatory halo. The halo disappeared soon leading to obliteration of the lips of the meatus with various degrees of constriction. In some cases a thin paper-like but firm diaphragm continuous with the lips of the meatus developed obliterating the orifice almost completely. Anterior urethroscopy revealed a few white plaques in the fossa navicularis and sometimes in other parts of the anterior urethra. Histological examination carried out on the sixteen cases showed all typical characteristics of lichen sclerosus et atrophicus. Out of sixteen cases two were associated with patches on the glans penis and one on the shaft of the penis. The condition is a peculiar variant of lichen sclerosus et atrophicus.

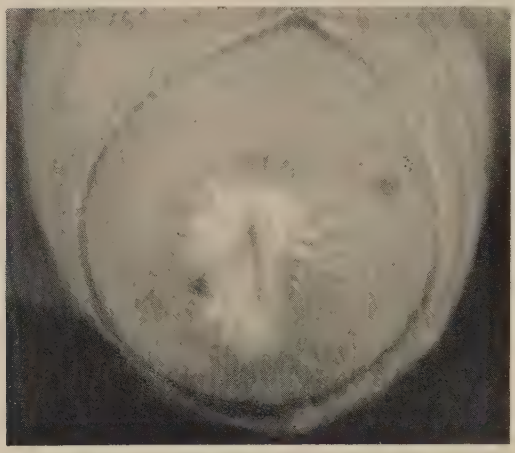

Fig. 1.

Reference.

Harkness, A. H. and Haber, H. (1957) *Proceedings XI International Congress on Dermatology*, 3, 1002.

The President : You would distinguish it from balanitis xerotica obliterans; is it not the same disease?

Dr. H. Haber : It is the same disease.

The President : Has anyone any views on balanitis xerotica obliterans as a distinct entity?

Dr. G. B. Dowling : I have always believed that balanitis xerotica obliterans is not an entity but an end result which may be produced by more than one process. A very chronic balanitis associated sometimes with a long prepuce and more or less phimosis, is one. In this type of balanitis the coronal sulcus is seen to be gradually obliterated long before the full picture of balanitis xerotica is realized. On the other hand similar meatal narrowing can of course be produced by lichen sclerosus.

The following cases have been published in *Proc. R. Soc. Med.*, **53**, 566.

Bisalbuminaemia with Curious Acrocyanotic Skin Changes.—Dr. D. I. Williams.

Darier's Disease Presenting with Dystrophy of the Nails. Dr. K. M. Harvey (for Dr. P. J. Hare).

The following cases were also shown :

Calcinosis Circumscripta Helicis.—Dr. D. I. Williams.

Anetoderma (Schweninger and Buzzi).—Dr. I. Sarkany (for Dr. D. I. Williams).

Polyarteritis Nodosa.—Dr. P. Hall-Smith.

Temporal Arteritis. Ischaemic Ulcers of the Scalp.—Dr. J. Everall (for Dr. G. B. Mitchell-Heggs).

Oil Melanosis.—Dr. C. Hodgson (for Dr. M. Feiwell).

Dr. W. Frain-Bell read a paper entitled "Grenz Rays in the Treatment of Benign Dermatoses".

17 March 1960.

Fibroepithelioma (Pinkus).—Dr. H. Gordon.

A man aged 65. retired.

History.—The patient has noticed a " raised piece of skin " on the back of his left upper arm all his life. He states that he scratched it about five years ago and that after this it increased in size. It has been, however, materially unaltered for the last five years. Recently he knocked it and an ointment was applied which made the whole condition irritable.

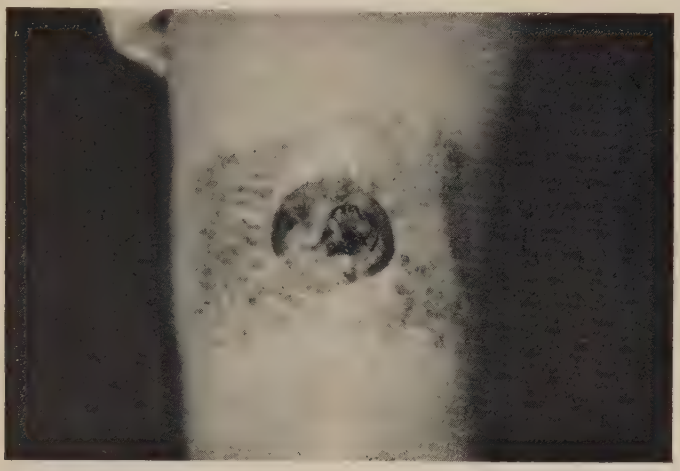

Fig. 1.

Clinical findings.—On the back of the left arm an area of what appeared to be contact dermatitis surrounding a slightly raised flat topped soft tumour approximately 3 cm. by 2 (Fig. 1). A few superficial erosions present on the surface.

Investigations.—Biopsy specimens taken. Reported on by Dr. Gowing, Royal Marsden Hospital, as follows :

" Sections show an epithelial tumour composed of anastomosing cords of basal cells separated by cellular fibrous tissue. In many fields the arrangement of the epithelium relative to the connective tissue is somewhat reminiscent of a fibroadenoma of the breast. These microscopic features are typical of the so-called fibroepithelioma of Pinkus". (Fig. 2.)

Comment.—The condition was apparently first described by Pinkus who reported four cases in 1953 (*Arch. Derm. Syph., Chicago*, **67**, 598). In his patients the tumours were multiple and gave the clinical impression of papillomas or sessile fibromas because they looked and felt fleshy, formed broad-based flat plaques or pedunculated elevations, and had a smooth or nodular surface without appreciable hyperkeratosis. Their colour was pink or reddish, in some instances with tinge of brown. One or two of the lesions had formed ulcerating tumours. He stated that he felt that these tumours did not constitute a truly new entity but rather that they are an unusual

variety of basal cell epithelioma. Pathological appearances appear to lie roughly half-way between a basal cell epithelioma and a seborrhoeic wart. Pinkus believed them to be innocent.

Dr. R. M. B. MacKenna : In his history this man said he had had some kind of lump " all his life " which I interpret as meaning a very long time, but until recently there has been no ulceration. Is the epitheliomatous element always present, or does it arise from a degenerative change in pre-existing (abnormal) tissue?

Dr. G. B. Dowling : Could not the lifelong lesion of which he speaks, have been a naevus (hamartomatous type) containing several elements one of which has finally proliferated to produce the present ulcerated tumour?

Dr. P. J. Hare : Could it possibly derive from the sweat apparatus? It resembles to my mind what one sees in some sweat duct tumours.

Dr. H. Haber : Fibro epithelioma of Pinkus is a clinical and histological entity. The lesions are multiple, look like little fibromas or seborrhoeic warts. The histology shows a characteristic reticulated pattern of epithelial structures which cytologically exhibit the features of a basal cell epithelioma. The tumour is surrounded by a dense cellular fibrous structure and could therefore be regarded as a hamartoma.

Fig. 2

Contact Dermatitis from Alcohol.—Dr. I. Martin-Scott.

A girl aged 19 years. Pathological technician.

History.— First seen four years ago with kerion of the leg. This was later treated with a coal tar bandage, which resulted in a contact dermatitis.

Next attended in August 1959 with contact dermatitis of neck, wrist and axilla due to a splash with ethyl alcohol—she stated she has been sensitive to all alcohols including scent, deodorants and alcoholic drinks for four years. There was also a history of skin trouble from earrings some years ago, and she wears suspenders with plastic clasps.

She occasionally drinks gin or vodka without any abnormal effects or flushing of the skin.

Clinical findings. —When first seen she had areas of contact dermatitis on the left

side of the neck and right wrist. Today there is acute swelling of the wrist due to deliberate contact with gin two days ago.

Investigations.—

Patch tests—1% ethyl alcohol in water	+
5% „ „ „ „	+
10% „ „ „ „	+
5% propyl „ „ „	(slight).
5% methyl „ „ „	„
Tar paste	„
Nickel sulphate	—
Neat gin	+

She had a more rapid reaction to the stronger strengths of alcohol.

Comment.—I suppose all of us at some time have been called into a surgical ward to see a case of obvious contact dermatitis around a clean surgical wound. We enquire about sensitizing antiseptics such as cetrimide, iodine flavine, Dettol, carbolic and mercury lotions, but sometimes we (or should I say I) draw a blank, as only surgical spirit was used. In the past I have dismissed this as a cause, but today I am not so sure that the occasional case may not have been due to alcohol sensitivity.

The present case was virtually a self diagnosis, by a sensible laboratory technician, and is the first case of this type I have encountered. I asked Dr. Calnan if he knew of any such cases, and he kindly referred me to a case reported by the late and deeply lamented Prof. Haxthausen in 1943, which had also been seen by the late Dr. Lomholt at an earlier date. Their case was a female medical student, who reacted by ingestion as well as contact with alcohol. Patch tests revealed that the optimum reaction was obtained when 10–20% ethyl alcohol was used.

In the present case, so far as I know, there are no abnormal symptoms after the intake of a small quantity of alcohol on special occasions, and on patch testing the higher the concentration the more rapid or severe the cutaneous reaction.

It is difficult to understand this type of sensitivity, and although I can offer no proof it seems possible to me that in this girl the alcohol causes the formation of foreign proteins in the skin to which the patient is sensitive—rather like Landsteiner's haptens.

She is also sensitive to coal tar, and I suppose it might be of interest to test her to the many fractions procured from tar, but I cannot see how this would help in attempting to desensitize the patient.

I should be interested to learn if any members have encountered similar cases, and suggestions on lines of further investigation and treatment would be appreciated, as this sensitivity is obviously going to be a great handicap to her in her career.

Lichen Aureus.—Dr. C. D. Calnan.

A man aged 23.

History.—Four years ago an eruption appeared over the right calf ; it was virtually maximal at the onset, and has not extended much subsequently.

Examination.—There is a group of flattened lichenoid papules over a small area of the right calf. They are situated in an area of orange-yellow or rusty coloured pigmentation, of which there are small outlying areas within a few inches.

Histology.—The epidermis looks normal. Separated by a band of normal connective tissue there is a well-defined infiltrate in the subpapillary layer consisting of round cells and histiocytes laden with haemosiderin. The capillaries show swollen endothelial cells leading to closure of their lumina (H. Haber).

Dr. G. B. Dowling : I think the name suggested is a good one until we know something more about the condition.

Dr. H. Haber : There is no doubt that the condition is a clinical and pathological entity. Clinically it represents lichenoid papules of a peculiar rusty colour. Microscopically it shows a

dense band of lymphocytic infiltration lying under the epidermis, but separted by a band of connective tissue. There is also a considerable amount of haemosiderin deposited within the histiocytes. The epidermis itself does not show any inflammatory changes. This is important to know as in other purpuric eruptions the epidermis shows spongiosis, immigration of round cells and presence of haemosiderin granules. At one of the meetings of the St. John's Hospital Society, I suggested the name lichen purpureus. I think "aureus" implies golden but the lesion is of a more rusty colour.

Dr. J. Everall: I have recently seen two similar cases, a father and son. The father was said to have had lesions for thirty years and the son, aged 25, for five years.

Dr. H. R. Vickers: I wish to thank Dr. Calnan for showing this case since I now know the diagnosis of a girl whom I first saw several months ago with two round lesions on the upper aspect of the shoulder which are very similar to the patient shown today. When I first saw her, from the shape of the lesions I wondered whether she could possibly have been biting herself and producing them in such a way, but on following her up at regular intervals it became apparent that this was a definite entity.

I am a little unhappy about the proposed name since this describes the colour of the lesions when it occurs in white people, and those of us who are now seeing many dark-skinned patients know how the colour of any lesion ceases to be of diagnostic help in these patients.

The following cases have been published in *Proc. R. Soc. Med.*, **53**, 568.

Livedo Reticularis.—Dr. Arthur Rook.

Cutaneous Arteriolitis.—Dr. R. H. Champion (for Dr. Arthur Rook).

Metastatic Carcinoma.—Dr. B. Schwartz.

Mycosis Fungoides.—Dr. H. Gordon.

Leucotrichia Annularis in Three Generations.—Dr. J. Savage.

Necrobiosis Lipoidica. Dr. M. A. Cowan (for Dr. R. E. Church).

Ringed Hair (Leucotrichia Annularis).—Dr. R. H. Champion and Dr. A. Rook.

Argyria.—Dr. I. Martin-Scott.

(1) **Chronic Dermatomyositis.** 2) **Rheumatoid Nodules.**—Dr. S. C. Gold.

Familial Benign Chronic Pemphigus with Chronic Staphylococcal Folliculitis.—Dr. J. Everall, Dr. R. Cairns and Dr. G. B. Mitchell-Heggs.

BOOK REVIEWS.

Dermal Angiology.*

This is an unusual and valuable book with a literary quality and a lively prose which commands attention and continued reading. It has a style indicating a very individual personality. Dr. Bean, who is a general physician, is obviously a dermatologist *manqué*, and should be received with acclamation in our ranks. Throughout his book there is the plea for the necessity of careful clinical observation and continued effort to correlate these observations with systemic disorders, functional or organic.

The theme of the book is the consideration of the vascular changes in the skin which are present as a result of heredity, trauma, age, hormonal or metabolic influences. The author emphasizes, in his preface, that " small lesions may help us to understand larger ones. . . . small vessels may illuminate a distant and seemingly unrelated obscurity." Dr. Bean, if he will allow me, recalls the poet who saw " all emotion in the trembling of a leaf and all the world in a grain of sand ".

Of course he is right in his preoccupation with disease of the small blood vessels of the skin, which are easily visible and recorded, and which are available for study in biopsy material and may reveal a significant pathology. Within the text are examples of the solid, down to earth humour that delights us in the American ; quotations, jingles and limericks bring home the point of an argument, but this light-heartedness does not disguise the dedication with which Dr. Bean has pursued the vascular spider over the past three decades. In the index are 31 references to his papers on the vascular spider and palmar erythema, to which the first 100 pages of the book are devoted. Dr. Bean was the first to relate these vascular anomalies with liver disease and pregnancy. His records cover the study of several thousands of patients and normal individuals.

There are numerous observations of interest, e.g. that spider naevi have been seen in the stomach and rectum and may be of prognostic value when associated with cirrhosis of the liver, fading in the patients who have recovered, presumably when the regenerated hepatic cells are once more capable of regulating the circulatory level of oestrogens. Again, he has noted enlargement of spider naevi three days before menstruation and for two or more days of the period.

There is a full account of the anatomy of the spider angioma but the diagrammatic representation was difficult to understand, insufficiently annotated, nor were the author's conclusions on his own histological material very clear, at least to me. Thus it is concluded that the artery of the spider :

(i) Arises from a single artery in the subcutis.
(ii) Arises by ectasia or metaplasia of an existing artery.
(iii) May be in some instances a modified glomus.

Further, Bean states that the spider in hepatic disease contains a coiled artery resembling the arteries of the endometrium, resulting from hyperplastic overgrowth of the vessel. He concludes that most typical spiders consist of a coiled artery with glomus cells in its walls, and that the white halo around the spider results from a rapid drainage of blood vessels through the arteriovenous shunt found in the subcutaneous tissue in the region of the spider. This description of the anatomy of the spider and shunt drainage was difficult to follow. Would not a large, pulsating

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* *Vascular Spiders and Related Lesions of the Skin.* William Bennett Bean (1959). Oxford : Blackwell Scientific Publications. Pp. 372. Price 63*s*.

artery draw off blood from the supplying vessel. lowering the pressure in the small vessels from the same channel, and therefore ensuring their collapse?

The incidence of spider naevi in children is given as 10–15% and it is stated that the natural evolution is not known. Dermatologists have, however, felt justified in assuring mothers that these spiders disappear spontaneously. Reference is made to the case shown by me at the Royal Society of Medicine in 1934. This was a woman with multiple spider naevi over the face and body appearing at the second month of numerous pregnancies. However, the observation that spiders may appear and fade with symptoms of a gastric ulcer was made by the late Dr. Henry McCormac who was in the chair and whose memory it gives me keen pleasure to recall. Dr. Bean's figures and charts reveal the incidence of spider naevi in pregnancy as 66% and he states that even iu the apparently normal skin, the dissecting microscope has revealed ectatic dilatation of skin capillaries in this proportion of pregnant women. Charts show the incidence of spider naevi in relation to the month of pregnancy and the month of the postpartum period, when they diminish in number. The difference in their occurrence between white and negro is startling : 69% of white and 11% of pregnant negresses. However, the palmar erythema is said to be three times as common in the pregnant negress. A racial predisposition may account for this difference in susceptibility of the small arteries to oestrogen levels, for, no doubt, the detection of the arterial spider on black skin does not offer difficulty to the experienced and careful observer. Palmar erythema is noted with rheumatoid arthritis and disseminated lupus erythematosus, but no details of the histopathology of the vessels is given. It is possible that the vessels would exhibit significant changes in their walls indicative of the disease. Dr. Bean also mentions the palmar and digital erythema, and clubbing of the fingers associated with cirrhosis of the liver, and suggests that increased blood flow is the cause of the clubbing. This may be so but oedema, if chronic, may be responsible for the soft tissue infiltration and hypertrophy. Recently, Hall (*Lancet*, i, 750, 1959) has suggested that clubbing of the fingers is due to dilatation of the canals of the glomus and that this will lead to permanent oedema.

A chapter is devoted to " carcinoid " and the accompanying angiomata which appear on the face. The affected vessels are described as proliferative and degenerative. Serotonin would appear to have a noxious effect on both the endothelium and vessel wall of small arteries.

Observation of many hundreds of cases of pellagra are of interest, for Dr. Bean has observed the abnormal reaction of the skin to friction and heat, and that light is only one of the physical stimuli that can expose abnormal status of the skin. There is consideration of the telangieiectasis occurring in Cushing's disease and the florid colour of the skin, but no mention is made of the deproteinization which may weaken the vessel wall and lead to ectasis and even purpura. Osler's disease is given 24 pages in the section on congenital and hereditary lesions. It is made clear that there is a developmental flaw in the structure of the muscle and connective tissue of the vessel walls. Small cavernous angiomata develop which are unable to contract and control bleeding when injured.

One small omission in the account of arteriovenous aneurysm is the absence of a description of the cutaneous signs, e.g. oedema of the hand and forearm, or ulceration of the foot, signs which may mimic artefacts. In the short section on infra-red photography, the captions of two photographs are transposed.

Dr. Bean is a clinical scientist and collector, and obviously an inspiring teacher. One concept which he repeats in his book is that there is a dynamism in structure and in the architectural fabric of the small blood vessels and a fluctuation in the patency of the functioning vascular bed which helps to explain the localization of vascular disease and perhaps the localization and morphology of patterns of skin reactions. The reader will gather that I read Dr. Bean's book with great interest and enjoyment and would recommend it to the notice of my colleagues in medicine.

L. F.

A New Atlas.*

Through the good offices of Messrs. Geigy, Professor Burckhardt has been able to produce a new atlas and manual including many colour illustrations. There is no doubt that some of the reproductions are absolutely first class, comparing favourably with the Graciansky atlas. Not all are up to this high standard and some of the black and white illustrations are only of moderate quality. Unfortunately the publishers have not always managed to include the relevant illustration next to the appropriate text and in some places these are separated by two or three pages. A few of the illustrations are of slightly unsuitable subjects for such an elementary book, notably the Bowen's disease of the ear which, though a beautiful picture, is not a characteristic lesion and the other, a half-tone of a mutilating rodent ulcer, so obviously a relic of the past.

The text is certainly up to date and brief. It is readable and orthodox. Treatment is biased towards the use of proprietary preparations especially those of American origin. Fortunately Dr. Peter Smith has been able to see that British preparations are given a hearing albeit somewhat brief. For the treatment of lupus vulgaris, calciferol is given pride of place over isoniazid. Notable omissions so far as illustrations are concerned include granuloma pyogenicum, cavernous haemangioma, and naevus flammeus.

This book must inevitably be compared with other available atlases; its price of £5 12*s*. 0*d*. certainly makes it a strong competitor with Semon and Wilson at £5 5*s*. 0*d*. and Percival and Dodds at £5 0*s*. 0*d*.

S. C. G.

Schoenfeld's Textbook of Dermatology and Venereology.†

The eighth edition of this popular German textbook was re-written by the author shortly before retiring from his teaching post at Heidelberg University. There is a useful new chapter on piles and special articles on antibiotics, sulphonamides, hormones and vitamins. The lay-out is attractive with an interesting short historical survey and diseases are listed according to aetiology, etc., as well as localization.

This textbook has been deservedly popular for the past twenty years with undergraduates and practitioners, and also as a reference book for specialists. It covers fully skin as well as venereal diseases with an additional interesting chapter on male sterility. It is up to date, the nomenclature, in particular the Latin and Greek, is impeccable and the paper and illustrations are first class.

Granuloma annulare is still, however, listed as a tuberculide, the connection between carcinoma and dermatomyositis is not mentioned and lichen sclerosus et atrophicus is considered to be a non-pruritic condition. Arsenic is said to have many beneficial properties and one feels that the dangers of prolonged therapy are not adequately stressed. It also advocates treating cavernous naevi vigorously at the earliest opportunity and the local application of penicillin, sulphonamides and antihistamines is not condemned.

In spite of these criticisms one is aware of the author's considerable experience throughout the book, which contains a wealth of useful information and practical hints.

J. M.

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* *Atlas and Manual of Dermatology and Venereology.* W. Burckhardt, edited and translated by S. Epstein (1960). London: Baillière Tindall and Cox. Pp. 276, colour plates 99, black and white illus. 73. Price £5 12*s*. 0*d*.

†*Lehrbuch der Haut und Geschlechtskrankheiten.* W. Schoenfeld (1959) 8th edition. Stuttgart: Georg Thieme Verlag. Pp. 546. 346 illus. Price DM.49. (£4 4*s*)

CURRENT LITERATURE.

THE PATHOGENESIS AND TREATMENT OF CHRONIC PARONYCHIA. J. Esteves. (1959) *Dermatologica, Basel*, **119**, 229.

The author describes the principal clinical characteristics of paronychia and reviews its pathogenesis, stressing the fact that the mechanisms of infection, trauma and prolonged immersion of the hands in water, are not sufficient to explain the chronic forms of the disease. He attributes fundamental importance to the nature of the host-medium, which reveals itself in these cases above all by peripheral vascular disturbances. He considers that paronychia is the result of the interaction of divers pathogenic factors, which he classifies under three headings : (i) predisposing factors : sex, peripheral circulatory disturbances with vascular instability, diminished resistance to infection ; (ii) precipitating factors : trauma, infection (pyogenic, mycotic) ; maintaining factors : occupation (immersion of the fingers, maceration, etc.), climate (sensitivity to cold), hormonal dysfunction (menopause, obesity, diabetes). The treatment of paronychia is logically based on consideration of the pathogenesis of each particular case, which should be studied in detail with a view to determining and evaluating the various factors which occasion it. All factors which tend to maintain the condition should be removed ; trauma should be avoided and the hands kept dry and warm, while at the same time the nail-fold should be disinfected with antiseptic powder and sometimes sealed with varnish. Good results are attributed to the use of x-ray therapy for diminishing the inflammatory reaction. It is absolutely necessary to seek to improve the peripheral circulation and to correct all the factors that may favour the disease which is often the first sign of important general changes in the life of the individual. (Author's summary.) J. F. S.

KERATOACANTHOMA MULTIPLEX. A. Burda and M. Piechocki. (1959) *Dermatologica, Basel*, **119**, 239.

The patient, a butcher, aged 52, had suffered since 1951 from fairly numerous lesions on his thighs, legs, elbows and forearms which varied in size from peppercorns to beans, were raised several millimetres above the normal skin-level and possessed horny caps or cores. They healed spontaneously in several months to several years, and left slight scars, which might be either pale or pigmented. The histological appearance seem consistent with the diagnosis of keratoacanthoma, though the authors at one point describe them as hyperplasia pseudo-epitheliomatosa. In their discussion they note the division of opinion in Britain and America as to whether "multiple self-healing epithelioma" is identical with multiple keratoacanthoma, without expressing an opinion of their own, and their citation of the literature is almost exclusively confined to keratoacanthoma. They rather faintheartedly exclude Grzybowski's case from their consideration, and do not seem to be aware of Witten and Zak's almost identical one. J. F. S.

SKIN DISEASE AMONG WORKERS WEEDING AND TRANSPLANTING RICE. F. Gianotti and R. Luvoni. (1958) *Giorn. ital. Derm.*, **99**, 377.

The labourers developed three main kinds of skin trouble all on the parts of the skin immersed n water : (i) Cercarial dermatitis. (ii) A non-specific papulo-pustular eruption attributed to the effects of maceration and trauma encouraging the entry of organisms. (iii) Interdigital fungous infections. A large part of the article is concerned with malacological parasitology.

A. L.

EOSINOPHILIC GRANULOMA OF THE SKIN AND ITS RELATIONSHIP TO LETTERER-SIWE RETICULO-ENDOTHELIOSIS AND HAND-SCHÜLLER-CHRISTIAN DISEASE. R. Vaccari and E. Manzini. (1958) *Giorn. ital. Derm.*, **99**, 425.

A woman with long-established diabetes insipidus had hyperplastic lesions of the groins and ano-genital region, and skiagrams showed translucencies of some of the bones and infiltration in the lungs. The histology of the accessible lesions showed a histiocytic infiltrate and many eosinophils. The authors regard this case as coming within the group of Hand-Schüller-Christian disease, Letterer-Siwe disease and eosinophilic granuloma of the bones, namely as a form of reticulosis. There is a very full bibliography. A. L.

TWO CASES OF CUTANEOUS CYLINDROMA (SPIEGLER'S TUMOUR). L. Rotelli. (1958) *Giorn. ital. Derm.*, **99**, 457.

In one the tumour was on the scalp and in the other on the thigh. A. L.

THE ANTIBODIES OF THE PLASMA FRACTIONS SEPARATED BY FLUSSOPHORESIS DURING THE COURSE OF HUMAN AND EXPERIMENTAL SYPHILIS. F. Ottolenghi-Lodigiani and U. Spagnoli. (1959) *Giorn. ital. Derm.*, **100**, 1.

Using a method of continuous paper electrophoresis the authors studied the course of antibody formation during the early stages of infection. The antibody response is more rapid and more vigorous in the rabbit than in man. A. L.

THE WAALER-ROSE REACTION AND THE L.E. PHENOMENON IN VARIOUS DERMATOSES WITH SPECIAL REFERENCE TO LUPUS ERYTHEMATOSUS. C. L. Meneghini and G. Cozza. (1959) *Giorn. ital. Derm.*, **100**, 30.

The Waaler-Rose reaction involves agglutination by the serum under investigation of sheep red cells that have been sensitized by rabbit anti-sheep serum. The authors found the test positive, that is with a titre greater than 1 in 64, in 3 out of 3 cases of acute L.E., 5 out of 7 cases of subacute L.E., and 3 out of 28 cases of chronic discoid L.E. It was also positive in 1 of 2 cases of symmetrical scleroderma, a single case of dermatomyositis, 2 out of 7 cases of erythema nodosum, 1 out of 10 cases of psoriasis and 1 out of 4 cases of pemphigus. Positive tests can be correlated with the active, inflammatory phase of the disease processes. The L.E. phenomenon was observed in 2 out of 3 cases of acute L.E. and in no other case. Figures are given in all the cases studied for plasma proteins and globulin fractions, E.S.R., tests for C reactive protein and heterophil haemagglutinins. A. L.

HYDROCORTISONE IN THE MANAGEMENT OF RECURRENT APHTHOUS STOMATITIS. Wilfred Sircus. (1959) *Brit. med. J.*, ii, 804.

Thirteen patients were placed on a double-blind treatment trial and observed for 12 months. One month after the initial consultation they were given a sequence of treatment with three lozenges, each being taken for one month. These consisted of a dummy preparation, an antibiotic and a combination of an antibiotic and prednisolone. After three months they were given an open trial of 28 days' treatment with hydrocortisone hemisuccinate linguets.

Three patients remained free from lesions after the initial consultation without any therapy. Three responded to the initial consultation but relapsed after 1 to 2 months. Dummy lozenges produced a reduction of over 50% in the frequency and duration of ulcers in 6 of the 13 subjects. Antibiotics were of no value but local application of a steroid produced a sustained remission in 25%. Suggestion and medical interest are shown to have important effects which must be allowed for in judging therapy in this disease. E. W.

GRISEOFULVIN TREATMENT OF ACUTE CATTLE RINGWORM INFECTIONS IN MAN. Thomas Cochrane and Adam Tullett (1959) *Brit. med. J.*, ii, 286.

Sixteen patients with *T. verrucosum* infections were treated with 1 to 2 g. of griseofulvin daily. The results were compared with 4 patients treated with fungicidals and antiseptic lotions. It was found that in acute inflammatory ringworm of the scalp and beard the duration of treatment was shortened by six weeks. E. W.

GRISEOFULVIN IN TREATMENT OF INFECTIONS OF SCALP DUE TO MICROSPORUM CANIS. Martin Beare and Donald Mackenzie. (1959) *Brit. med. J.*, ii, 1137.

Nineteen children with *M. canis* infection of the scalp were treated with 0·25 g. of griseofulvin three times daily for periods of 3½ to 10 weeks. There were no toxic effects. Hairs ceased to fluoresce under Wood's Light after 3 weeks' treatment, but fungus could be recovered from hairs and debris for several weeks, and therefore 3 to 4 negative cultures, taken at weekly intervals, are necessary before concluding that an individual is free from infection. In the majority continuous treatment protects newly-formed hair from invasion but interrupted or inadequate treatment results in reinfection from superficial and intrafollicular debris. Detailed study of one unusual case revealed a well-established infection in non-fluorescent portions of hairs. This suggests that there may be a differential absorption of Griseofulvin dependent on the relative rate of growth of hair.

Gruseofulvin therapy alone failed to eradicate infection and removal of infected debris from the scalp is necessary. No fresh lesions occurred during treatment and it is suggested that griseofulvin may be of the greatest possible value in protecting contacts. E. W.

GRISEOFULVIN IN TREATMENT OF PERSISTENT FUNGAL INFECTIONS OF THE SKIN. A. J. E. Barlow, F. W. Chattaway, G. K. Hargreaves and C. J. La Touche. (1959) *Brit. med. J.*, ii, 1141.

Thirty-four patients with fungal infections of the skin were treated with griseofulvin in a dosage of 1 to 2 g. daily for periods of 3 to 20 weeks. Twenty-six had long-standing *T. rubrum* infection of skin and nails. Three were unable to tolerate the drug on account of nausea, dizziness and an erythematous rash. Leucopenia occurred in 4 out of 12 patients in whom regular blood counts were done but in no instance did the absolute count fall below 2000.

The response to treatment of *T. rubrum* infection of skin depends on the rate of desquamation of keratin. Infections of smooth skin cleared in 10 to 14 days, and of palms and soles in 35 to 42 days. In contrast the response to treatment of nails depends on the rate of nail growth, and 4 months must be allowed for infection of fingernails to grow out, and over a year would be required for toenails.

It is suggested that a combination of surgical removal of nails with griseofulvin systematically and topical fungicidals offer the patient suffering from nail infection with *T. rubrum* the best chance of cure. E. W.

TOXIC EPIDERMAL NECROLYSIS IN A CHILD. J. V. F. Catto. (1959) *Brit. med. J.*, ii, 544.

An example of this rare condition in a child aged 3, who made a complete recovery after treatment with antibiotics and corticosteroids. The syndrome is thought to be due to a toxaemia of unknown origin and no common factor linking other reported cases can be suggested.

E. W.

DERMABRASION FOR THE IMPROVEMENT OF ACNE SCARS. H. Rattner and P. Lazar. (1959) *J. Amer. med. Ass.*, **171**, 2326.

This is a report to the Committee on Cosmetics, from those who have had several years' experience of dermabrasion with modern technique. It seems clear that dermabrasion is the best method available for treating acne scars, though certain types of scarring are not improved. The common and unsightly deep pitted acne with patulous follicles and uneven leathery skin is unsuitable for treatment. Types of scarring are well illustrated and the report gives useful information on case selection and on technique of dermabrasion. G. C. W.

GRISEOFULVIN FOR THE SYSTEMIC TREATMENT OF DERMATOMYCOSES. H. Blank, J. G. Smith, F. J. Roth and N. Zaias. (1959) *J. Amer. med. Ass.*, **171**, 2168.

Griseofulvin was given by mouth to 200 patients with superficial dermatomycoses (mainly *T. rubrum* infections). The usual dose was 1 g. per day. Results were good and no serious toxic effects were encountered. G. C. W.

TOXICOLOGICAL STUDIES AND EFFECTIVENESS OF GRISEOFULVIN IN DERMATOMYCOSES. C. H. McCuistion, M. G. Lawlis and B. B. Gonzales. (1959) *J. Amer. med. Ass.*, **171**, 2174.

Thirty-two patients (mostly children) with tinea (predominantly of the scalp) were treated with oral griseofulvin in doses of from $\frac{1}{2}$ to 1 g. daily. Twelve of the children had *T. tonsurans* infection. Results were good and there were no serious toxic effects. An increase in the proportion of mature lymphocytes was found in the peripheral blood. G. C. W.

USE OF TRANQUILLIZERS IN DERMATOLOGY. W. Wright. (1959) *J. Amer. med. Ass.*, **171**, 1642.

Nine different drugs (rauwolfia alkaloids, chlorpromazine group, meprobamate, hydroxyzine and oxanamide) were given to patients with dermatoses (psoriasis, ano-genital pruritus, lichen planus, atopic dermatitis, chronic urticaria, localized neurodermatitis and nummular eczema). The study was based on 740 patients and in 75% of them the " blind " method of drug selection was used. Side effects were common and included urticaria, the erythemata, purpura, stomatitis

and pityriasis rosea-like eruptions. There were a few serious complications (convulsions, agranulocytosis and syncope). The general impression was that these drugs were of little use for the treatment of the dermatoses studied, with the exception of nummular eczema which seemed to respond to hydroxyzine hydrochloride. G. C. W.

PROPHYLACTIC ADMINISTRATION OF ANTIBIOTICS IN PATIENTS RECEIVING STEROIDS SYSTEMICALLY. R. C. Gibbs, L. Biro and M. B. Sulzberger. (1960) *J. Amer. med. Ass.*, **172**, 11.

This clinical impression is based on consideration of patients admitted to the dermatological service of the Bellevue Hospital over a 9 months' period. The impression was that those patients on steroid therapy who at the same time received prophylactic antibiotics subsequently developed more staphylococcal infection than those who received no antibiotics. G. C. W.

GIANT PIGMENTED NAEVI. J. L. Russell and R. G. Reyes. (1959) *J. Amer. med. Ass.*, **171**, 2083.

This is thought to have been the largest pigmented naevus to have been excised and grafted successfully. It occupied the whole of the back in a girl aged 18, and appears to have been of the "Tierfell" kind. Numerous small pigmented naevi had to be removed from donor sites before grafts were taken. G. C. W.

NAEVUS ELASTICUS IN DISSEMINATED TUMOURS. P. de Graciansky and R. Leclercq. (1960) *Ann. Derm. Syph., Paris*, **87**, 5.

The term "naevus elasticus" includes two distinct groups—"naevus elasticus regionis mammariae" of Lewandowsky and a second group to which the authors add three more cases here to the five described in the literature. Characteristically the lesions develop insidiously at any age from infancy, as yellowish-white small flat papules especially on the thighs, and lower back. Histologically orcein-stained sections show increase and thickening of the elastic fibres in the middle and deeper dermis. They believe the condition is quite distinct from pseudo-xanthoma elasticum and refer briefly to other connective tissue naevi. F. F. H.

ACQUIRED PSEUDO-ICHTHYOSIS IN CIRCULAR SPOTS. M. Ito and T. Tanaka. (1960) *Am. Derm. Syph., Paris*, **87**, 26.

About 150 cases of this condition have been described in Japan and a few in neighbouring countries. It consists of circular well-defined scaling plaques with rather an ichthyosiform surface; the plaques vary in size from a few to dozens. They are situated chiefly on the trunk though they can be on the limbs and are symptomless. They may improve temporarily in summer and in some cases ordinary ichthyosis is also present; there has sometimes been improvement with vitamin A. The differential diagnosis and possible aetiology are discussed; the authors believe it is possibly related to ichthyosis. F. F. H.

LICHEN PLANUS AND CORTICO-STEROIDS. Jorge Homez. (1960) *Ann. Derm. Syph., Paris*, **87**, 44.

Two of three cases treated with cortisone were cured and both of those treated with prednisolone were cured. F. F. H.

CONGENITAL HIPPOCRATIC FINGERS WITH PALMO-PLANTAR HYPERKERATOSIS AND BONY TROUBLES. Y. Bureau, H. Barrière and M. Thomas. (1959) *Ann. Derm. Syph., Paris*, **86**, 611.

The authors describe two patients who showed clubbing of the fingers and toes associated with a palmar and plantar hyperkeratosis and large stature with diminished density of the bones. In one case three other members of the same generation were affected. They discuss various types of clubbing and eventually conclude that their cases present a peculiar association which should be placed in Touraine's group of "polykeratoses". F. F. H.

CHRONIC DISSEMINATED NODULAR ENDARTERITIS ASSOCIATED WITH OBSTRUCTIVE JAUNDICE. F. Sannicandro. (1959) *Ann. Derm. Syph., Paris*, **86**, 623.

A man aged 70 with long-standing jaundice presented hemispherical hyperkeratotic itching papules which developed slowly into pigmented scars. The lesions were due to a primary arteritis

which provoked a necrobiosis of the hair follicles and their appendages. The relation to various forms of thromboangiitis obliterans are discussed; the jaundice may be a visceral manifestation of the same process. F. F. H.

THE STATE OF THE CARDIOVASCULAR SYSTEM IN CHRONIC LUPUS ERYTHEMATOSUS. L. Bugaro, A. Leoni and W. Selmi. (1959) *Giorn. ital. Derm.* **100**, 39.

There were ECG changes in 7 out of 12 cases of up to five years' standing and 14 out of 23 with a longer history. Depression of ST and alterations of the T-wave were a feature of the second group. In no case was there clinical evidence of cardiac failure. The possible effects of drugs on the tracings do not seem to have been considered. A. L.

THE BEHAVIOUR OF SOME NON-SPECIFIC TESTS IN BURNED PATIENTS. F. Allegra. (1959) *Giorn. ital. Derm.*, **100**, 48.

The tests were: (1) E.S.R. (2) Plasma proteins. (3) Electrophoresis of plasma proteins. (4) Electrophoresis of total glycoprotein. (5) Electrophoresis of Schiff-positive glycoprotein. (6) C-reactive protein.

A rise in the E.S.R. occurs some time after 24–48 hours and is preceded by the appearance of C-reactive protein. The gamma globulin rises late after an initial fall. The alpha two moiety behaves similarly in tests 3, 4 and 5, and shows a late rise and slow fall to normal with complete healing, by which time the E.S.R. and C-reactive protein have returned to normal values. A. L.

KYRLE'S DISEASE. P. Nazzaro, G. C. Fuga and G. Bignami. (1959) *Giorn. ital. Derm.*, **100**, 65.

A description of unusually widespread lesions which spared only the palms, soles, part of the face, interscapular region and the nails. There were papules within the mouth, and oedema and erythema of the genitalia. A table of the 37 cases reported up to 1958 is included. A. L.

THE HEALING PROPERTIES OF A NEW PREPARATION. A. Mancosu. (1959) *Giorn. ital. Derm.*, **100**, 92.

"Solcuseryl" is made from the blood of calves. It is said to promote the uptake of oxygen by tissues and to have been used for treating peptic ulcers. The author used it for chronic leg ulcers and gave it chiefly intramuscularly and intravenously. The photographs show healing which was rapid by any standard, and which is said to have proceeded over the whole ulcer floor, not merely from the edges, and to have produced sound, supple scars. The investigation was unfortunately quite uncontrolled but the clinical impression conveyed is impressive. A. L.

ACRODERMATITIS ENTEROPATHICA. F. Gianotti. (1959) *Giorn. ital. Derm.*, **100**, 154.

A 19-month-old boy with the typical disease. *Candida albicans* was isolated from the stools and there was a disturbance of fat metabolism consisting of difficulty in dealing with larger lipoprotein molecules. One million units of nystatin by mouth daily was well tolerated and an immediate clinical improvement occurred but follow-up was impossible. A. L.

INVOLVEMENT OF THE NERVOUS SYSTEM IN ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS. V. Musumeci. (1959) *Giorn. ital. Derm.*, **100**, 163.

Psychotic and neurological manifestations can occur either as an integral part of the disease, probably as a result of vascular lesions, or as a result of toxaemia or treatment. The author has made a special study of this aspect of the disease and has provided four illustrative cases and a bibliography of 77 references. A. L.

CUTANEOUS FIBRO-EPITHELIOMA OF PINKUS. A. Toti. (1959) *Giorn. ital. Derm.*, **100**, 189.

A case of the kind described by Pinkus (1953) *Arch. Derm., Chicago*, **67**, 598 as pre-malignant fibro-epithelial tumours of the skin. A. L.

THERAPEUTIC ACTIVITY OF A POWDER CONTAINING PROTEIN LYSATES AND CHLORAMPHENICOL. G. Armuzzi. (1959) *Giorn. ital. Derm.*, **100**, 199.

The powder was well tolerated by 23 patients who had it applied to leg ulcers or exudative eczema. Three patients could not tolerate the burning sensation which the powder provoked, though none showed objective signs of hypersensitivity. It seemed fairly effective for the ulcers but the results were uncontrolled. A. L.